Human Neural Stem Cell Transplantation Ameliorates Radiation-Induced Cognitive Dysfunction.

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Authors: M M Acharya, L A Christie, M L Lan, E Giedzinski, J R Fike, S Rosi, C L Limoli

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Public Summary:
Cranial radiotherapy induces progressive and debilitating declines in cognition that may, in part, be caused by the depletion of neural stem cells. The potential of using stem cell replacement as a strategy to combat radiation-induced cognitive decline was addressed. Unbiased stereology revealed that 23% and 12% of the engrafted cells survived 1 and 4 months after transplantation into a model of radiotherapy, respectively. Engrafted cells migrated extensively, differentiated along glial and neuronal lineages, and expressed the activity-regulated cytoskeleton-associated protein (Arc), suggesting their capability to functionally integrate into the hippocampus. These data show that hNSCs afford a promising strategy for functionally restoring cognition in irradiated animals which could be a prelude to developing clinical trials in humans.

Scientific Abstract:
Cranial radiotherapy induces progressive and debilitating declines in cognition that may, in part, be caused by the depletion of neural stem cells. The potential of using stem cell replacement as a strategy to combat radiation-induced cognitive decline was addressed by irradiating athymic nude rats followed 2 days later by intrahippocampal transplantation with human neural stem cells (hNSC). Measures of cognitive performance, hNSC survival, and phenotypic fate were assessed at 1 and 4 months after irradiation. Irradiated animals engrafted with hNSCs showed significantly less decline in cognitive function than irradiated, sham-engrafted animals and acted indistinguishably from unirradiated controls. Unbiased stereology revealed that 23% and 12% of the engrafted cells survived 1 and 4 months after transplantation, respectively. Engrafted cells migrated extensively, differentiated along glial and neuronal lineages, and expressed the activity-regulated cytoskeleton-associated protein (Arc), suggesting their capability to functionally integrate into the hippocampus. These data show that hNSCs afford a promising strategy for functionally restoring cognition in irradiated animals. Cancer Res; 71(14); 1-12. (c)2011 AACR.

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